36. (New) A method as claimed in Claim 28 wherein the first biological sample is from a diseased cell type and the second biological sample is from a corresponding cell type unaffected by the disease.

37. (New) A method as claimed in Claim 29 wherein the first biological sample is from a diseased cell type and the second biological sample is from a corresponding cell type unaffected by the disease.

Remarks

In the Office Action mailed October 21, 2002, the claims were divided into five groups, Group I, claims 1, 3-8, and 11-16, drawn to a method of making an array of anti-ligands; Group II, claims 2, 9, and 10, drawn to a method of isolating a ligand; Group III, claims 17, 21, 23, and 25, drawn to a use of the array; Group IV, claims 18, 22, 24, and 26, drawn to a use of an identical array; and Group V, claims 19 and 20, drawn to a use of an array using fluorescent reporters.

In response, applicants elect Group I, claims 1, 3-8, and 11-16, with traverse.

The Examiner has stated that the "inventions" of groups I and II relate to two distinct methods of making an array of anti-ligand and a ligand with a tagging agent isolated from the anti-ligand. The Examiner asserts that different method steps and/or end results are produced by each method. In view of the amended claims, the claims directed to groups I and II do not provide for different method steps and/or different end results.

New claims 27 and 28, and claims dependent thereon, provide proper linkages *via* a use obtained by the method as claimed.

Election of Species

The Office Action also required election of a species from among 1) antibody; 2) antigen binding variant or derivative; and 3) nucleic acid. The Examiner has stated that each of the foregoing species differs in structure and the method to make and assay each of these compounds involve different reagents and/or steps that result in different products. In response, applicants elect for examination "antigen binding variant or derivative" without traverse.

It is understood that upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 C.F.R. 1.141.

Applicants also traverse the restriction requirement as currently set forth for the following reasons. To be valid, a restriction requirement must establish both that (1) the "inventions" are either independent or distinct, and (2) that examination of more than one of the "inventions" would constitute a burden to the Examiner. The claims, as amended, relate to one or more specific arrays and are capable of being used together.

Favorable consideration of claims 1-13 and 27-37 is earnestly solicited.

Respectfully submitted,

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Date: December 23, 2002
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Certificate of Mailing Under 37 C.F.R. § 1.8(a)

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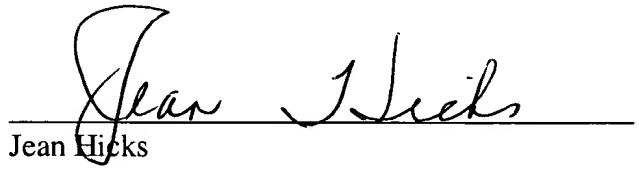

Jean Hicks

Date: December 23, 2002

Marked Up Version of Amended Claims

Pursuant to 37 C.F.R. § 1.121(c)(1)(ii)

1. A method of making an array of selected anti-ligands comprising:

(i) providing a library of anti-ligand molecules displayed for binding with a ligand on the surface of a replicable unit;

(ii) providing a mixture of ligands;

(iii) exposing the library to the mixture whereby ligand/anti-ligand binding can take place;

(iv) isolating and amplifying the number of anti-ligands which bind ligands; and

(v) applying a preparation of the same anti-ligands, or a plurality of different anti-ligands, to a separate region of a substrate to form an array of separate anti-ligand-containing regions on a solid support.

2. (Amended) A method as claimed in Claim 1, [further comprising a step of isolating ligands bound to anti-ligands on the surface of the replicable units between steps (iii) and (iv)] wherein the ligands in the mixture are immobilized.

3. (Amended) A method as claimed in Claim 1, wherein the [ligands in the mixture are immobilized] mixture of ligands is separated on the basis of one or more parameters before it is exposed to the library.

4. (Amended) A method as claimed in Claim [1] 3, wherein the mixture of ligands is separated [on the basis of one or more parameters before it is exposed to the library] using two-dimensional gel electrophoresis.

5. (Amended) A method as claimed in Claims 4 wherein the [mixture of] ligands [is separated using two-dimensional gel electrophoresis] in the separated mixture are immobilized on a support surface.

6. (Amended) A method as claimed in Claim 5, wherein the [ligands in the separated are immobilized on a] support surface is a nitrocellulose or polyvinylidene difluoride (PVDF) membrane.

7. (Amended) A method as claimed in Claim [6] 5 wherein the support surface is a [nitrocellulose or polyvinylidene difluoride (PVDF) membrane] replica of the two dimensional gel and is used directly in step (iii) of the method of Claim 1.

8. (Amended) A method as claimed in Claim [6] 1, wherein the [support surface is a replica of the two-dimensional gel and is used directly in step (iii) of the method of Claim 1] anti-ligand comprises a protein or polypeptide.

9. (Amended) A method as claimed in Claim [2] 8 wherein the [ligands in the mixture are tagged by a tagging agent so that they can be isolated by an anti-tagging agent which binds to the tagging agent] anti-ligand is an antibody or an antigen binding variant or derivative thereof.

10. (Amended) A method as claimed in Claim [9] 1 wherein the [tagging agent is biotin and the anti-tagging agent is avidin] anti-ligand is a nucleic acid.

11. (Amended) A method as claimed in claim 1 wherein the [anti-ligand comprises a protein or polypeptide] identity of at least some of the ligands and/or anti-ligands is unknown.

12. (Amended) A method as claimed in Claim 11 wherein the [anti-ligand is an antibody or an antigen binding variant or derivative thereof] identity of substantially all of the ligands and/or anti-ligands is unknown.

13. (Amended) A method as claimed in claim 1 wherein [the anti-ligand is a nucleic acid] 10 to 50 different anti-ligands are applied per region of the array.

Please cancel claims 14-26.

27. (New) A method of isolating ligands comprising

(i) providing a library of anti-ligand molecules displayed for binding with a ligand on the surface of one or more replicable units;

(ii) providing one or more compounds to be screened as ligands;

(iii) exposing the compounds to the library of anti-ligand molecules whereby ligand/anti-ligand binding can take place;

(iv) isolating the compounds which bind to the anti-ligands.

28. (New) A method comprising providing an array made by a method comprising (i) providing a library of anti-ligand molecules displayed for binding with a ligand on the surface of one or more replicable units;

(ii) providing one or more compounds to be screened as ligands; and

(iii) exposing the compounds to the library of anti-ligand molecules whereby ligand/anti-ligand binding can take place;

further comprising

comparing the presence, absence and/or amount of one or more ligands in first and second biological samples by detecting differences in ligand/anti-ligand binding when the array is exposed to the samples.

29. (New) A method comprising providing an array made by a method comprising (i) providing a library of anti-ligand molecules displayed for binding with a ligand on the surface of one or more replicable units;

(ii) providing one or more compounds to be screened as ligands; and

(iii) exposing the compounds to the library of anti-ligand molecules whereby ligand/anti-ligand binding can take place;

comprising comparing the presence, absence and/or amount of one or more ligands in first and second biological samples by detecting differences in ligand/anti-ligand binding when an array is exposed to the first biological sample and a substantially identical array is exposed to the second biological sample.

30. (New) A method as claimed in Claim 28 wherein the ligands in the first and second biological samples are labeled with different first and second fluorescent reporters so that, in use, under examination of the array under conditions of fluorescence excitation, anti-ligands in the array which are bound predominantly to ligands from one of the first and second biological samples give a first or second fluorescence emission; and anti-ligands which bind substantially equal numbers of ligands from the first and second biological samples give a combined fluorescence emission.

31. (New) A method as claimed in Claim 29 wherein the ligands in the first and second biological samples are labeled with different first and second fluorescent reporters so that, in use, under examination of the array under conditions of fluorescence excitation, anti-ligands in the array which are bound predominantly to ligands from one of the first and second biological samples give a first or second fluorescence emission; and anti-ligands which bind substantially equal numbers of ligands from the first and second biological samples give a combined fluorescence emission.

32. (New) A method as claimed in Claim 28 wherein the first and second biological samples are applied to identical but separate arrays of anti-ligands.

33. (New) A method as claimed in Claim 29 wherein the first and second biological samples are applied to identical but separate arrays of anti-ligands.

34. (New) A method as claimed in Claim 28 wherein the mixture of ligands provided in step (ii) of the method of making the array is derived from the same source as the first or second biological sample.

35. (New) A method as claimed in Claim 29 wherein the mixture of ligands provided in step (ii) of the method of making the array is derived from the same source as the first or second biological sample.

36. (New) A method as claimed in Claim 28 wherein the first biological sample is from a diseased cell type and the second biological sample is from a corresponding cell type unaffected by the disease.

37. (New) A method as claimed in Claim 29 wherein the first biological sample is from a diseased cell type and the second biological sample is from a corresponding cell type unaffected by the disease.

Clean Version of Amended Claims
Pursuant to 37 C.F.R. § 1.121(c)(1)(ii)

1. A method of making an aray of selected anti-ligands comprising:

(i) providing a library of anti-ligand molecules displayed for binding with a ligand on the surface of a replicable unit;

(ii) providing a mixture of ligands;

(iii) exposing jthe library to the mixture whereby ligand/anti-ligand binding can take place;

(iv) isolating and amplifying the number of anti-ligands which bind ligands; and

(v) applying a preparation of the same anti-ligands, or a plurality of different anti-ligands, to a separate region of a substrate to form an array of separate anti-ligand-containg regions on a solid support.

2. (Amended) A method as claimed in Claim 1, wherein the ligands in the mixture are immobilized.

3. (Amended) A method as claimed in Claim 1, wherein the mixture of ligands is separated on the basis of one or more parameters before it is exposed to the library.

4. (Amended) A method as claimed in Claim 3, wherein the mixture of ligands is separated using two-dimensional gel electrophoresis.

5. (Amended) A method as claimed in Claims 4 wherein the ligands in the separated mixture are immobilized on a support surface.

6. (Amended) A method as claimed in Claim 5, wherein the support surface is a nitrocellulose or polyvinylidene difluoride (PVDF) membrane.

7. (Amended) A method as claimed in Claim 5 wherein the support surface is a replica of the two dimensional gel and is used directly in step (iii) of the method of Claim 1.

8. (Amended) A method as claimed in Claim 1, wherein the anti-ligand comprises a protein or polypeptide.

CLEAN VERSION OF AMENDED CLAIMS PURSUANT TO 37 C.F.R. § 1.121

9. (Amended) A method as claimed in Claim 8 wherein the anti-ligand is an antibody or an antigen binding variant or derivative thereof.

10. (Amended) A method as claimed in Claim 1 wherein the anti-ligand is a nucleic acid.

11. (Amended) A method as claimed in claim 1 wherein the identity of at least some of the ligands and/or anti-ligands is unknown.

12. (Amended) A method as claimed in Claim 11 wherein the identity of substantially all of the ligands and/or anti-ligands is unknown.

13. (Amended) A method as claimed in claim 1 wherein 10 to 50 different anti-ligands are applied per region of the array.

27. (New) A method of isolating ligands comprising

(i) providing a library of anti-ligand molecules displayed for binding with a ligand on the surface of one or more replicable units;

(ii) providing one or more compounds to be screened as ligands;

(iii) exposing the compounds to the library of anti-ligand molecules whereby ligand/anti-ligand binding can take place;

(iv) isolating the compounds which bind to the anti-ligands.

28. (New) A method comprising providing an array made by a method comprising

(i) providing a library of anti-ligand molecules displayed for binding with a ligand on the surface of one or more replicable units;

(ii) providing one or more compounds to be screened as ligands; and

(iii) exposing the compounds to the library of anti-ligand molecules whereby ligand/anti-ligand binding can take place;

further comprising

comparing the presence, absence and/or amount of one or more ligands in first and second biological samples by detecting differences in ligand/anti-ligand binding when the array is exposed to the samples.

29. (New) A method comprising providing an array made by a method comprising (i) providing a library of anti-ligand molecules displayed for binding with a ligand on the surface of one or more replicable units;

(ii) providing one or more compounds to be screened as ligands; and

(iii) exposing the compounds to the library of anti-ligand molecules whereby ligand/anti-ligand binding can take place;

comprising comparing the presence, absence and/or amount of one or more ligands in first and second biological samples by detecting differences in ligand/anti-ligand binding when an array is exposed to the first biological sample and a substantially identical array is exposed to the second biological sample.

30. (New) A method as claimed in Claim 28 wherein the ligands in the first and second biological samples are labeled with different first and second fluorescent reporters so that, in use, under examination of the array under conditions of fluorescence excitation, anti-ligands in the array which are bound predominantly to ligands from one of the first and second biological samples give a first or second fluorescence emission; and anti-ligands which bind substantially equal numbers of ligands from the first and second biological samples give a combined fluorescence emission.

31. (New) A method as claimed in Claim 29 wherein the ligands in the first and second biological samples are labeled with different first and second fluorescent reporters so that, in use, under examination of the array under conditions of fluorescence excitation, anti-ligands in the array which are bound predominantly to ligands from one of the first and second biological samples give a first or second fluorescence emission; and anti-ligands which bind substantially equal numbers of ligands from the first and second biological samples give a combined fluorescence emission.

32. (New) A method as claimed in Claim 28 wherein the first and second biological samples are applied to identical but separate arrays of anti-ligands.

33. (New) A method as claimed in Claim 29 wherein the first and second biological samples are applied to identical but separate arrays of anti-ligands.

34. (New) A method as claimed in Claim 28 wherein the mixture of ligands provided in step (ii) of the method of making the array is derived from the same source as the first or second biological sample.

35. (New) A method as claimed in Claim 29 wherein the mixture of ligands provided in step (ii) of the method of making the array is derived from the same source as the first or second biological sample.

A2

36. (New) A method as claimed in Claim 28 wherein the first biological sample is from a diseased cell type and the second biological sample is from a corresponding cell type unaffected by the disease.

CLEAN VERSION OF AMENDED CLAIMS PURSUANT TO 37 C.F.R. § 1.121

37. (New) A method as claimed in Claim 29 wherein the first biological sample is from a diseased cell type and the second biological sample is from a corresponding cell type unaffected by the disease.

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